AMENDMENTS TO THE CLAIMS

Listing of claims

- 1.-84. (Canceled)
- 85. (Previously Presented) An isolated human antibody or functional fragment thereof that specifically binds an epitope of CD38 (SEQ ID NO: 22), wherein said antibody or functional fragment thereof mediates killing of a CD38+ target cell by antibody dependent cellular cytotoxicity with at least five-fold better efficacy than chimeric OKT10 antibody (SEQ ID NOS: 23 and 24) under the same or substantially the same conditions when a human PBMC cell is employed as the effector cell, wherein said CD38+ target cell is selected from the group consisting of LP-1 (DSMZ: ACC41) and RPMI-8226 (ATCC: CCL-155), and wherein the ratio of effector cells to target cells is between about 30:1 and about 50:1.
- 86. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 85, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 5 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 13.
- 87. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 85, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 6 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 14.
- 88. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 85, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 7 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 15.
- 89. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 85, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 8 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 16.
- 90. (Cancelled)
- 91. (Previously Presented) An isolated antibody to according to claim 85, which is an IgG.

- 92. (Previously Presented) An isolated antibody to according to claim 91, which is an IgG1.
- 93. (Previously Presented) An isolated human antibody or functional fragment thereof that specifically binds to an epitope of CD38 (SEQ ID NO: 22), wherein said antibody or functional fragment thereof mediates killing of a CD38-transfected CHO cell by cell dependent cytotoxicity with at least two-fold better efficacy than chimeric OKT10 antibody (SEQ ID NOS: 23 and 24) under the same or substantially the same conditions.
- 94. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 93, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 5 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 13.
- 95. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 93, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 6 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 14.
- 96. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 93, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 7 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 15.
- 97. (Cancelled)
- 98. (Currently Amended) An isolated antibody to according to <u>claim elaims</u> 93, which is an IgG.
- 99. (Previously Presented) An isolated antibody to according to claim 98, which is an IgG1.
- 100. (Previously Presented) An isolated human or humanized antibody or functional fragment thereof comprising an antigen-binding region that competes for binding with an antibody which specifically binds to an epitope of CD38, wherein the epitope comprises an amino acid residue between 1 to 215 of CD38 (SEQ ID NO: 22).

- 101. (Previously Presented) An isolated antibody or functional fragment thereof of claim 100, wherein the epitope comprises an amino acid residue found within amino acids 44-66, 82-94, 142-154, 148-164, 158-170, or 192-206 of CD38 (SEQ ID NO: 22).
- 102. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 100, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 5 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 13.
- 103. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 100, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 6 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 14.
- 104. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 100, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 7 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 15.
- 105. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 100, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 8 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 16.
- 106. (Cancelled)
- 107. (Previously Presented) An isolated antibody according to claim 100, which is an IgG.
- 108. (Previously Presented) An isolated antibody according to claim 107, which is an IgG1.
- 109. (Previously Presented) An isolated human antibody or functional fragment thereof that specifically binds to CD38, comprising a property selected from the group consisting of:
 - (a) an EC50 of less than or equal to 100 nM;
 - (b) antagonizes lymphocyte proliferation as well as chOKT10 antibody;
 - (c) antagonizes IL-6 release as well as chOKT10;
 - (d) mediates the killing of CD34+/CD38+ precursor cells by antibody dependent

- cellular cytotoxicity better than chOKT10; and
- (e) is cross-reactive with cynomolgus CD38 and rhesus monkey CD38.
- 110. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 109, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 5 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 13.
- 111. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 109, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 6 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 14.
- 112. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 109, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 7 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 15.
- 113. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 109, comprising an H-CDR1, H-CDR2 and H-CDR3 depicted in SEQ ID NO: 8 and an L-CDR1, L-CDR2 and L-CDR3 depicted in SEQ ID NO: 16.
- 114. (Cancelled)
- 115. (Previously Presented) An isolated antibody according to claim 109, which is an IgG.
- 116. (Previously Presented) An isolated antibody according to claim 115, which is an IgG1.
- 117. (Previously Presented) A pharmaceutical composition comprising an antibody or functional fragment thereof according to claim 85 and a pharmaceutically acceptable carrier or excipient therefor.
- 118. (Withdrawn) A method for treating a disorder or condition associated with the undesired presence of CD38+ cells, comprising administering to a subject in need thereof an effective amount of the pharmaceutical composition according to claim 117.

- 119. (Withdrawn) A method according to claim 118, wherein said disorder or condition is a haematological disease.
- 120. (Withdrawn) A method according to claim 118 selected from the group consisting of multiple myeloma, chronic lymphocytic leukemia, chronic myelogenous leukemia, acute myelogenous leukemia, and acute lymphocytic leukemia.
- 121. (Withdrawn) A method according to claim 118, wherein said disorder or condition is an inflammatory disease.
- 122. (Withdrawn) A method according to claim 121 selected from the group consisting of rheumatoid arthritis and systemic lupus erythematosus.
- 123. (Withdrawn) An isolated epitope of CD38 consisting essentially of an amino acid sequence selected from the group consisting of amino acids 44-66, 82-94, 142-154, 148-164, 158-170, 192-206 and 202-224 of CD38 (SEQ ID NO:22).
- 124. (Withdrawn-Currently Amended) The isolated epitope of CD38 according to <u>claim</u> elaims 123, consisting of an amino acid sequence selected from the group consisting of amino acids 44-66, 82-94, 142-154, 148-164, 158-170, 192-206 and 202-224 of CD38 (SEQ ID NO:22).
- 125. (Withdrawn-Currently Amended) A kit comprising (a) one or more isolated epitope(s) of CD38 according to claim 123 124; (b) an antibody library and (c) instructions for use.
- 126. (Previously Presented) A variable heavy chain of an isolated antibody or functional fragment thereof that is encoded by (i) a nucleic acid sequence comprising SEQ ID NO: 1, 2, 3, or 4, or (ii) a nucleic acid sequences that hybridizes under high stringency conditions to the complementary strand of SEQ ID NO: 1, 2, 3, or 4, wherein said antibody or functional fragment thereof is specific for an epitope of CD38.
- 127. (Previously Presented) A variable light chain of an isolated antibody or functional fragment thereof that is encoded by (i) a nucleic acid sequence comprising SEQ ID NO: 9, 10, 11, or 12, or (ii) a nucleic acid sequences that hybridizes under high stringency conditions to the complementary strand of SEQ ID NO: 9, 10, 11, or 12,

- wherein said antibody or functional fragment thereof is specific for an epitope of CD38.
- 128. (Withdrawn) An isolated nucleic acid sequence that encodes an antigen-binding region of a human antibody or functional fragment thereof that is specific for an epitope of CD38.
- 129. (Withdrawn) The nucleic acid sequence of claim 128, encoding a variable heavy chain of an isolated antibody or functional fragment thereof, which comprises (i) a sequence selected from the group consisting of SEQ ID NOS: 1, 2, 3 and 4 or (ii) a nucleic acid sequence that hybridizes under high stringency conditions to the complementary strand of SEQ ID NO: 1, 2, 3 or 4, wherein said antibody or functional fragment thereof is specific for an epitope of CD38.
- 130. (Withdrawn) The nucleic acid sequence of claim 128, encoding a variable light chain of an isolated antibody or functional fragment thereof, which comprises (i) a sequence selected from the group consisting of SEQ ID NOS: 9, 10, 11 and 12 or (ii) a nucleic acid sequence that hybridizes under high stringency conditions to the complementary strand of SEQ ID NO: 9, 10, 11 or 12, wherein said antibody or functional fragment thereof is specific for an epitope of CD38.
- 131. (Withdrawn) A vector comprising a nucleic acid sequence according to claim128.
- 132. (Withdrawn) An isolated cell comprising a vector according to claim 131.
- 133. (Withdrawn) An isolated cell according to claim 135, wherein said cell is bacterial.
- 134. (Withdrawn) An isolated cell according to claim 133, wherein said cell is mammalian.
- 135. (Withdrawn) A method for targeting CD38+ cells in a subject or a cell sample, comprising the step of allowing said CD38+ cells to be contacted with an antibody or functional fragment thereof according to claim 1.

- 136. (Withdrawn) A method of isolating a human or humanized antibody or functional fragment thereof comprising an antigen binding region which specifically binds to an epitope of CD38, comprising:
 - a) contacting said epitope of CD38 with an antibody library; and
 - b) isolating said antibody or functional fragment thereof,

wherein said epitope is a linear epitope.

- 137. (Withdrawn) A method according to claim 136, wherein said linear epitope comprises amino acid residues 192-206 of CD38.
- 138. (Withdrawn) A method of isolating a human or humanized antibody or functional fragment thereof comprising an antigen binding region which specifically binds to an epitope of CD38, comprising:
 - a) contacting said epitope of CD38 with an antibody library; and
 - b) isolating said antibody or functional fragment thereof,

wherein said epitope is a conformational epitope.

- 139. (Withdrawn) A method according to claim 138, wherein said conformational epitope comprises one or more amino acid sequences selected from the group consisting of amino acids 44-66, 82-94, 142-154, 148-164, 158-170, and 202-224 of CD38.
- 140. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 31, which comprises a heavy chain amino acid sequence selected from the group consisting of (i) SEQ ID NO: 6; and (ii) a sequence having at least 60 percent sequence identity in the CDR regions with the CDR regions depicted in SEQ ID NO: 6.
- 141. (Previously Presented) An isolated antibody or functional fragment thereof according to claim 140, which comprises a light chain amino acid sequence selected from the group consisting of (i) SEQ ID NO: 14; and (ii) a sequence having at least 60 percent

sequence identity in the CDR regions with the CDR regions depicted in SEQ ID NO: 14.